REMARKS

This response accompanies a Request for Continued Examination of this application and responds to the Official Action dated June 5, 2009.

Applicants sincerely thank Examiner Kumar for discussing this case with Applicants' counsel by telephone on September 17, 2009. The Examiner has entered an interview summary into the record. Please note that the additional counsel present on the phone for applicants during the telephone interview was Robert G. McMorrow, Jr. (not Roberte Makowski).

Claim 49 is corrected as suggested on page 2 of the Official Action. Claims now pending are 1, 5, 8-11, 13, 15, 18-19, 29, 32, 47 and 49. Withdrawal of the previous claim objections and the rejections under 35 U.S.C. 112 is acknowledged with appreciation.

All claims remain provisionally rejected for obviousness-type double patenting over certain claims of co-pending application Ser. No. 11/251,208. This rejection is respectfully traversed, in view of the amendment to the claims of both this application and the co-pending '208 application. The rejection was initially based upon the 100% identity between SEQ ID NO: 3 and 4 of this application and SEQ ID NO: 51 and 52 of the co-pending '208 application. See, Official Action of 1/25/07, page 6. As now amended, the co-pending '208 application claims make no reference to SEQ ID NO: 51 and 52, but instead recite SEQ ID NO: 64 and 65 and variants having at least 95% identify. As shown from the attached alignments between the sequences of SEQ ID NO: 3 of the present application and SEQ ID NO: 64 of the '208 application, or the alignment between the encoded polypeptide sequences (SEQ ID NO: 4 and SEQ ID NO: 65), they share only less than 10% sequence identity. Since the rationale supporting the provisional double patenting rejection has now been mooted by amendment of the claims in the co-pending '208 application, and the claims of the present application would not have been obvious from the current claims of the '208 application, the obviousness type double patenting rejection should be withdrawn.

All claims remain rejected under 35 U.S.C. § 103 over Lanahan et al. in view of Gan, Grant et al. and Samuelson et al. Submitted in support of traversal of this rejection is the Declaration of Dr. Gerhard Ritte.

The primary reference to Lanahan teaches the expression of transgenic thioredoxin in plants for the purpose of achieving enhanced protein/starch recovery. As recognized in the Official Action, the nucleic acids recited in the present claims (GRX2 nucleic acids) are not disclosed. Lanahan does not teach transgenic plants with an increased tolerance to an environmental stress associated with any of salinity, drought, or low temperature. The thioredoxin proteins disclosed by Lanahan are different from the GRX2 protein recited in the pending claims. Ritte Declaration, ¶ 7.

The Gan reference is cited as disclosing SEQ ID NO: 3 and SEQ ID NO: 4. The reference contains no suggestion to produce transgenic plants with an increased tolerance to an environmental stress associated with any of salinity, drought, or low temperature. Gan discloses no transformation experiments and provides no suggestion as to the expected phenotype of plant cells or plants transformed with a yeast GRX2 nucleic acid. Ritte Declaration, ¶ 7.

Samuelson is relied upon for teaching that yeast genes produce an expected phenotype when expressed in plants. Samuelson discloses expression of two yeast Fe(lll) reductases - FRE1 and FRE2 - in Nicotiana tabacum. Samuelson analyzed the effect of a simple Fe(lll) reductase transformation on the Fe(lll) reduction in plants and the Fe concentration in leaves. It was shown that, if a foreign Fe(lll) reductase is introduced into tobacco, then Fe(lll) reduction is enhanced. Samuelson relates to genes distinct from GRX2 and the skilled person would not accept from Samuelson's disclosure a categorical statement that expression of a yeast gene in a plant always produces an expected phenotype. See Ritte Declaration, ¶ 7 and footnote 6.[1]

Grant is the most relevant of the cited references in terms of whether the claimed phenotype could have been predicted. Ritte Declaration, ¶ 7. Grant found that expression of both GRX1 and GRX2 increased in response to oxidative stress, heat stress and osmotic stress. Ritte Declaration, ¶ 9. The experiments identified the responsible promoter elements, but Grant's experiments did not involve expressing a full-length GRX2 gene product. Ritte Declaration, ¶¶

[1] The statement in the Official Action that Samuelson teaches that "yeast genes can be successfully expressed in plants to obtain expected phenotype" is an over-generalization. An obviousness analysis is fact-based, and a conclusion of obviousness must be based on the facts of a particular case and not generalities. *In re Freed*, 165 USPQ 570, 571 (CCPA 1970).

9-11. Grant did not specifically test for any of the stresses recited in claim 1, which are related to, but distinct from, the oxidative stress, heat stress and osmotic stress analyzed in Grant's experiments. Ritte Declaration, ¶ 13.[2]

The stress response mechanism in both plants and yeast is highly complex. Ritte Declaration, ¶ 14. The glutaredoxin system in plants is apparently more complex than the yeast glutaredoxin system, since plants contain many more glutaredoxin genes. Ritte Declaration, ¶ 15. Plants are overall physiologically different than yeast. Ritte Declaration, ¶ 16. All of these factors suggest unpredictability.

From the above, the cited prior art would not have provided a reasonable expectation that expression of a yeast GRX2 gene in a plant would increase tolerance to salinity, drought, and/or low temperature stress. At most, the prior art suggests the possibility of achieving that result. Ritte Declaration, ¶ 17.

Obviousness requires not a mere possibility of success, but a reasonable expectation of success. Page 7, lines 1-6 of the Official Action make clear that the rejection is premised upon an "obvious to try" standard. It is important to keep in mind that most experimentation is

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[2] Earlier in the prosecution of this application, the Examiner took a position that: "The specification provides guidance on increasing low temperature, salt or dehydration stress tolerance of a transgenic plant or a plant expressing the nucleic acid sequence of SEQ ID NO: 3. However, the specification does not provide guidance on increasing stress tolerance to said transgenic plant cell or plant under any type of environmental stress condition other than low temperature, salt and dehydration stresses. In the absence of guidance, undue experimentation would have been required by a skilled artisan to determine how to use the instantly claimed transgenic plant cell or plant comprising SEQ ID NO: 3, in a method of increasing tolerance of said plant cell or plant to any type of environmental stress." Official Action of 1/25/2007, at pages 11-12.

Implicit in the rejection asserting that undue experimentation would be needed to confer tolerance to stresses other than low temperature, salt or dehydration stresses is a finding that providing tolerance to other stresses would have been unpredictable. In response to the rejection of the claims as non-enabled, Applicants amended to claims to recite tolerance to low temperature, salt or dehydration stresses (compare claim 1 as filed to current claim 1).

To avoid prejudice to Applicants, since unpredictability has been asserted earlier, the "law of the case" doctrine should apply to preclude finding that response to specific stresses in Grant (oxidative, heat, osmotic) would be predictive of response to the different stresses recited in claim 1 (salinity, drought, low temperature).

undertaken with some expectation of success. This idea was expressed in a recent decision by the Court of Appeals for the Federal Circuit in *Abbott Laboratories v. Sandoz, Inc.,* 544 F.3d 1341 (Fed. Cir. 2008) as follows:

> "The evaluation of the choices made by a skilled scientist, when such choices lead to the desired result, is a challenge to judicial understanding of how technical advance is achieved in the particular field of science or technology. Such understanding is critical to judicial implementation of the national policy embodied in the patent statute. In *Publication of Tomlinson*, 53 C.C.P.A. 1421, 363 F.2d 928 (1966) our predecessor court discussed the role of "obvious to try" in scientific and technologic research and in patentability: 'Slight reflection suggests, we think, ***that there is usually an element of 'obviousness to try' in any research endeavor, that is not undertaken with complete blindness but rather with some semblance of a chance of success, and that patentability determinations based on that as the test would not only be contrary to statute but result in a marked deterioration of the entire patent system as an incentive to invest in those efforts and attempts which go by the name of 'research.'*** *Id.* at 931. The Court in *KSR* did not create a presumption that all experimentation in fields where there is already a background of useful knowledge is "obvious to try," without considering the nature of the science or technology. The methodology of science and the advance of technology are founded on the investigator's educated application of what is known, to intelligent exploration of what is not known. Each case must be decided in its particular context, including the characteristics of the science or technology, its state of advance, the nature of the known choices, the specificity or generality of the prior art, and the predictability of results in the area of interest . . . . The district court concluded that it was not predictable, from the *in vitro* behavior of azithromycin, how any specific clarithromycin extended release formulation would perform *in vivo*." (emphasis added)

Denial of patent protection by overemphasis on the "obvious to try" rationale would stifle research into, and disclosure of, important and useful discoveries where the skilled artisan would not have seen a reasonable expectation of success. In *Application of Antonie*, 559 F.2d 618 (CCPA 1977) the court explained:

> "The PTO and the minority appear to argue that it would always be obvious for one of ordinary skill in the art to try varying every parameter of a system in order to optimize the effectiveness of the system even if there is no evidence in the record that the prior art recognized that particular parameter affected the result. As we have said many times, obvious to try is not the standard of 35 U.S.C. s 103. *In re Tomlinson*, 363 F.2d 928, 53 CCPA 1421, 150 USPQ 623 (1966). Disregard for the unobviousness of the results of "obvious to try" experiments disregards the "invention as a whole" concept of [section] 103, *In re Dien*, 371 F.2d 886, 54

> CCPA 1027, 152 USPQ 550 (1967) and *In re Wiggins*, 397 F.2d 356, 55 CCPA 1356, 158 USPQ 199 (1968), and ***overemphasis on the routine nature of the data gathering required to arrive at appellant's discovery, after its existence became expected, overlooks the last sentence of [section] 103.*** *In re Saether*, 492 F.2d 849, 181 USPQ 36 (CCPA 1974)." (emphasis added; footnotes omitted)

For these reasons, the "obvious to try" rationale should not be applied to the facts of this case. The above authority suggests that proper application of the "obvious to try" idea requires more of an expectation of success than a mere possibility.[3] The rejection under 35 USC § 103 should be withdrawn and patent protection accorded to this invention.

CONCLUSION

For the above reasons, Applicants respectfully request withdrawal of the rejections, and indication that the application is allowable. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a two-month extension of time to respond to the Office Action mailed June 5, 2009, and a Request for Continued Examination with the required fee payment. No further fees are believed due. If any additional fee is due, please

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[3] See also, *Ex Parte Toru Taniguchi*, 2008 WL 3874455 (PTO Bd. App. Int. 2008)("... the Examiner's position amounts to an argument that it would have been obvious for one of ordinary skill in the art to try various protrusion distances, including any within the range claimed. But 'obvious to try is not the standard of 35 U.S.C. § 103.' *Antonie*, 559 F.2d at 620 (citing *In re Tomlinson*, 363 F.2d 928 (CCPA 1966)). 'The controlling question is simply whether the differences ... between the prior art and appellant's invention as a whole are such that appellant's invention as a whole would have been obvious.'(Id.) *KSR* recognized that '[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.' *KSR*, 127 S.Ct. at 1732. In such circumstances, "the fact that a combination was obvious to try might show that it was obvious under § 103.' *Id.* ... The mere possibility that one would try to protrude the wafer to a distance extending to one falling within the claimed range does not demand a conclusion of obviousness where one of ordinary skill in the art would have no expectation of successfully obtaining a useful wafer. 'To have a reasonable expectation of success, one must be motivated to do more than merely to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.' *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed.Cir.2006)(internal quotations omitted)."

charge our Deposit Account No. 03-2775, under 13311-00012-US from which the undersigned is authorized to draw.

Respectfully submitted,

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Attachments: Sequence Alignments using ClustalW with default parameters.
Declaration of Dr. Gerhard Ritte, with attachments.

CLUSTAL 2.0.12 multiple sequence alignment

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SIN3            ATGGAGACCAATTTTTCCTTCGACTCGAATTTAATTGTTATTATCATTATCACGTTGTTT 60
SIN64           ATGGCGTATAATCAAGAAGATAGTAAAAGACTATCAGACA--AGTATAAGAAGGAGGGAC 58
                **** *   ***                *   **   *  *  *  ** *  * *  *

SIN3            GCCACAAGAATTATTGCTAAAAGATTTTTATCTACTCCA-AAAATGGTATCCCAGGAAAC 119
SIN64           ATTTTGACAAGT-TGAAAAGAGAAATATTGTCTAACCCATGGAATAATACAGAAGAGAAT 117
                      * ** * *    * *  * * ** ****  ***   ***  **    **  **

SIN3            AGTTGCTCACGTAAAGGATCTGATTGGCCAAAAGGAAGTGTTTGTTGCAGCAAAGACATA 179
SIN64           AGTGAATCTTTTGAACAAGCGCTTCGG---AAAAGAGTTGCCAGTACTGTTAAAGAAATG 174
                ***   **   * **  * *   * **   *** **  **   **       ***** **

SIN3            -CTGCCCTTACTGTAAAGCTACTTTGTCTACCCTCTTCCAAGAATTGAACGTTCCCAAAT 238
SIN64           GTTAACGAAGATGAAGAATTAATATTTAAAAACAGAGGGCTAACCAGTGCATTGATTGAA 234
                  *  *     ** * *  ** * * *  *  *         *   *  * **     *

SIN3            CCAAGGCCCTTGTGTTGGAATTAGATGAAA-TGAGCAATGGCTCAGAGATTCAAGACGCT 297
SIN64           TCACAATTGGTCAAGGACAACTACCTAAAGCTGGGTAGTAAAATGGAGGGGGATAATGGT 294
                 **       *       ** **  * **  ** * * *      ***    *  * * *

SIN3            -----TTAGAAGAAATCTCGGGCCAAAAAACTGTACCTAACGTATACATCAATGGCAAGC 352
SIN64           GATGGTGAGAAGAAATTT---GACTTGGATGTCTATGTACGGTCTAAGTTACAGGATCCC 351
                     * ********* *   * *    *  * **  **  ** **  * *  **    *

SIN3            ACATTGGTGGTAACAGCGATTTGGAAACTTTGAAGAAAAATGGCAAGTTAGCTGAAATAT 412
SIN64           AAACTATTGGAAATGATAAAGGGACAACTTC-AGGAAACACTGAACTCTTATGAAGAGGA 410
                * * *  *** **     *   *  *****  * **** *  * *   *     * *

SIN3            TGAAGCCGGTATTTCAATAG 432
SIN64           AGCAAATGGAAGTACGTAA- 429
                 * *   ** * * *   *
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CLUSTAL 2.0.12 multiple sequence alignment


SIN4            METNFSFDSNLIVIIIITLFATRIIAKRFLSTPKMVSQETVAHVKDLIGQKEVFVAAKTY 60
SIN65           MAYNQE-DSKRLSDKYKKEGHFDKLKREILSNPWNNTEENSESFEQALRKR----VASTV 55
                *  * . **: :     .      : :.:**.*   ::*.   .:: : ::    .*.*

SIN4            CPYCKATLSTLFQELNVPKS--KALVLELDEMSNGSEIQDALEEISGQKTVPNVYINGKH 118
SIN65           KEMVNEDEELIFKNRGLTSALIESQLVKDNYLKLGSKMEGDNGDGE-KKFDLDVYVR-SK 113
                    :   . :*:: .:..:  :: ::: : :. **:::.   : . :*   :**:. .:

SIN4            IGGNSDLETLKKNGKLAEILKPVFQ------ 143
SIN65           LQDPKLLEMIK--GQLQETLNSYEEEANGST 142
                : . . ** :*  *:* * *:.  :
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